

REMARKS/ARGUMENTS

The disclosure has been amended to correspond to the changes made to the parent application.

With respect to the deposit information for plasmid pD2 RF-HN (ATCC 75388), it is stated in the specification that the deposit of the plasmid is made under the provisions of the Budapest Treaty on December 17, 1992 (see page 12 of specification). A copy of the deposit form is enclosed. In addition, it is hereby stated, under the signature of the undersigned, that all restrictions on the deposit will be removed upon grant of a patent on this application or precursor application. In the latter respect, the issuance of U.S. Patent No. 5,968,776 is noted. In addition, non-viable deposits will be replaced by the applicant.

In the Office Action of February 21, 2004, in the parent case, the Examiner had objected to the amendment to the sequence of Figure 5, also effected herein, as constituting new matter. The changes made are to the nucleotide at positions 540 and 630 and to the resulting amino acid at the position corresponding to 630 of the nucleic acid sequence. The Examiner considered each of these changes to constitute new matter. It is the applicant's position that the changes correct clerical errors and do not involve new matter. In any event, the changes to the amino acid sequence, at the position corresponding to site 630 of the nucleic acid sequence is consequential correction to site 630.

Figures 5A to 5E show the nucleotide sequences and deduced amino acid sequences for the respiratory syncytial virus fusion (RSV F) protein. Shortly after the grand-parent application was filed, it was discovered that, in preparing the Figure, certain nucleotides, at positions 540 and 630, were transcribed in error. A Preliminary Amendment was submitted with this application to correct the errors in Figure 5B.

The change of "T" to "C" at position 540 leads to a change of the complementary nucleotide from "A" to "G". The change of "G" to "A" at position 630 leads to a change in the complementary nucleotide "C" to "T". This change also

leads to a change of the amino acid encoded by the codon including position 630 from "ARG" to "GLN".

Thus, applicants seek to change the identification of two nucleotides, the other changes being consequential on the change of identification of the two nucleotides.

The errors are clerical in nature, arising from transcription of the sequences for inclusion in the grand-parent application. It has always been possible to correct clerical errors in patent specifications and, indeed, Examiner's habitually ask applicants to check their specification in order to detect and correct clerical errors. No one derives any benefit from an erroneous specification, neither applicants nor the public. As noted above, the Examiner in the parent applications characterize the changes that applicant has made as new matter.

The corrections sought to be made to the sequences are quite different from those decided as new matter in the *Ex parte Maizel*, 27 USPQ2d p1664 and are akin to the changes permitted in *Ex parte Marsili*, 214 USPQ p.904. A copy of each of these decisions is enclosed for convenience.

In *Ex parte Maizel*, the errors sought to be corrected arose in the original sequencing of the DNA coding sequence, which came to light upon resequencing. The original sequencing contained errors which lead to frame shifting and an erroneous encoded amino acid sequence. By way of contrast, applicants had already expressed the RSV F gene and, indeed, correctly presented the sequence in the priority GB 9200117.1. A copy of that GB specification is of record in the parent application, but is enclosed for convenience.

It is clear that the corrections are minor, being two in number and giving rise to only a single amino acid change. The single amino acid difference is unlikely to have any affect on the functionality of the protein. As applicants state in the specification, the nucleotide sequence encoding the RSV F given in Figures 5A to 5D differs by approximately 1.8% divergence in the coding sequences, resulting in

eleven amino acid substitutions (square boxes in Figures 5A to 5E; page 15, lines 15 to 18), from a published sequence of the RSV F gene.

As mentioned above, the applicants were already in possession of the DNA encoding the RSV F protein at the time of filing of their priority GB 9200117.1. The nucleotide and amino acid sequences are set forth in the priority application in Figure 5 and a restriction map of the gene is shown in Figure 6 of the priority application. The same comparison analysis as is set forth in this application is set forth therein (see page 4, lines 32 to 35 and Figure 5). Figure 5 in the GB application correctly shows the sequence sought to be corrected by the Amendments made.

A scientific paper was published in the August 12, 1994 edition of Biotechnology, after the effective filing date of this application, describing the scientific work which is the basis for the patent application. A copy of the scientific paper is of record in the parent application, but is attached for convenience. In connection with that scientific paper, there was submitted to GenBank on September 23, 1993, after the effective filing date of this application, the nucleic acid and encoded amino acid sequences for the RSV F protein. A copy of the GenBank deposit is of record, but a further copy is enclosed for convenience.

The sequences shown in the GenBank deposit are the same as those filed with the priority GB application and do not contain the errors present in Figure 5B and sought to be corrected. It is submitted that the sequences that form part of the GB application and the GenBank deposit constitute collateral evidence that the changes are corrections of errors. In the Advisory Action dated July 29, 2003, the Examiner comments that:

"Applicants could just as easily discovered a sequence error in the foreign priority document and corrected them for filing of the US application."

This scenario is highly unlikely, since the GenBank deposit, made after this filing, contains the same sequences as the foreign priority document and applicant is seeking to correct the sequence presented in this application.

In addition, the specification describes the preparation of plasmid pD2RF-HN in Example 9 of the specification. Such plasmid was deposited with ATCC on December 17, 1992, before the effective filing date of this application, under accession number 75388 (see page 12, lines 27 to 43).

As described in Example 9, the RSV F gene lacking the transmembrane domain and cytoplasmic tail was linked to the PIV-3 HN gene devoid of the hydrophobic anchor domain and cloned into baculovirus expression vector pD2 to provide plasmid pD2 RF-HN. As is seen from Figure 5, the portion of the RSV F nucleotide sequence that is present in the deposited plasmid encompasses that where the corrections are sought to be made. A person sequencing the RSV F gene from plasmid pD2 RF-HN would discover the errors in the sequences shown in Figure 5B.

As determined by the Federal Circuit in the *Enzo Biochem Inc. v. Gen-Probe Incorporated et al* [63 USPQ2d p1609], a deposit of a biological material constitutes an adequate description of the deposited material sufficient to comply with the written description requirement of 35 USC 112, first paragraph. A copy of the Decision is enclosed for convenience. Accordingly, the specification as filed contains a written description of the portion of the sequence that is sought to be corrected.

In the parent application, the Examiner relied solely on MPEP 608 for his objection, quoting:

"All amendments or claims must find descriptive basis in the original disclosure, or they involve new matter."

It is submitted that this statement is not intended to deal with corrections of all types, since corrections are routinely permitted by the Office.

Ex parte Maizel recognizes this principle:

“We recognize that errors may well arise in the sequencing of DNA and that a mechanism for correcting such errors in the Patent and Trademark Office is highly desirable”

If such errors could not be corrected because of MPEP 608, then there would be no need for the Board to express a desire for a mechanism of correction.

The Board goes on to state:

“Unfortunately, no general rule can be established because the question of whether or not a change in the chemical structure of a DNA sequence set forth in the specification is permitted depends on the facts of each case and the significance of the modification to both the subject matter *claimed*, i.e., the *invention*, and the subject matter *described* in the specification.” (emphasis in original)

Thus, the Board indicated there could be no general rule, but did recognize that a change to a DNA sequence may be permitted, depending on the facts of the situation and the significance of the modification. The Board certainly did not consider that such changes to correct errors were proscribed by MPEP 608.

The facts surrounding the Examiner’s rejection in the parent application are quite different from that in *Ex parte Maizel*. In *Maizel*, the error arose in the sequencing itself, only discovered on resequencing. In this case, the sequencing had been done, as evident from the priority GB application, and the error later arose in transcribing the sequence for the grand-parent application.

In *Ex parte Marsili*, the applicants were permitted to change the chemical structure of a compound as set forth in claim 1 thereof. A more refined investigation of the structure of the compound showed that a hetrocyclic ring, depicted as saturated, was unsaturated at two locations in the ring. This correction was permitted.

Formal drawings have been substituted for the informal drawings. It is noted that Figure 5 has been amended as shown on the enclosed print of the

original drawing in red, to correct a spelling error. The Sequence Listing enclosed herewith, both in hard copy and computer-readable form, includes the changes effected in the drawings.

It is hereby stated that the hard copy and computer-readable form of the Sequence Listing are the same.

The claims have been amended in the interests of expedited prosecution. In this regard, it is noted that the definition of the chimeric protein is the same as allowed in the diagnostic claims of the grand-parent case. The claims directed to the hybrid gene and method of making the chimeric protein recombinantly utilizes corresponding language.

The PTO-1449 submitted herewith lists all prior art cited by or to the PTO in the parent and related filings since copies of each of the references have been provided in the parent application, no copies are enclosed herein.

Respectfully submitted,



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Attachments.